

## CLAIMS

1. A composition useful as an ultrasound contrast agent comprising microbubbles encapsulating a gas within a shell made from intermolecular regions of blended compounds, said compounds comprised of polar head groups linked to straight-chained hydrophobic groups of differing chain lengths said hydrophobic chains oriented toward the gas phase, whereby the longer chain lengths assemble beneath the shorter chains thereby stabilizing the shell.

2. The composition of Claim 2 wherein the bipolar compounds have the structure:

$R_1-X-Z$ ;

$R_2-X-Z$ ;

and  $R_3-X-Z'$

where  $R_1$ ,  $R_2$  and  $R_3$  are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyldisulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where  $R_1$  is greater than  $R_2$  and  $R_1$  is greater than or equal to  $R_3$ ;  $R_3$  has one or more such hydrophobic groups having the same or different lengths; X is a linker connecting the hydrophobic group to the polar head group; Z is a polar head group selected from the group consisting of  $CO_2-M^+$ ,  $SO_3^-M^+$ ,  $SO_4^-M^+$ ,  $PO_3^-M^+$ ,  $PO_4^-M^+$ ,  $N(R)_4^+$ , a pyridinium or substituted pyridinium group, and a zwitterionic group; R is selected from the group consisting of -H, -CH<sub>3</sub>, alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and Z' is a nonionic group.

3. The composition of Claim 2 wherein  $R_1$ ,  $R_2$  and  $R_3$  are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

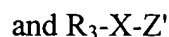
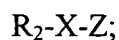
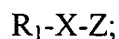
4. The composition of Claim 2 wherein X is selected from the group consisting of -  
 $(\text{CH}_2)_m^-$ ,  $-(\text{CH}_2)_m\text{CO}_2(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{CONH}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{NHCONH}(\text{CH}_2)_n^-$ ,  
 $-(\text{CH}_2)_m\text{OCONH}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{O}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{NH}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{N}[(\text{CH}_2)_m]_2^-$ ,  
 $-(\text{CH}_2)_m\text{S}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m^-$ ,  $-(\text{CH}_2)_m\text{SO}(\text{CH}_2)_n^-$ ,  $-(\text{CH}_2)_m\text{SO}_2(\text{CH}_2)_n^-$ ,  
 $-(\text{CH}_2)_m\text{NH}(\text{CH}_2)_n\text{CO}_2(\text{CH}_2)_o^-$ ,  $-[(\text{CH}_2)_m]_2\text{N}(\text{CH}_2)_n\text{CONH}(\text{CH}_2)_o^-$ , where m, n, and o are the  
same or different and are less than 5, DL-lysine, aspartic acid, glutamic acid, serine, cysteine,  
homocysteine, cystine, serinol, itaconic acid, tigilic acid, maleic acid, DL-malic acid, succinic  
acid, tartaric acid, malonic acid, citric acid, phthalic acid, terephthalic acid, N,N-bis[2-  
hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-hydroxyethyl)glycine, 3-[N,N-bis(2-  
hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-tris[hydroxymethyl]methyl-3-  
aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine.

5. The composition of Claim 2 wherein Z' is selected from the group consisting of  
polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides,  
polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and composites thereof.

6. The composition of Claim 2 wherein Z' is poly(ethyleneglycol) with the number  
of ethyleneglycol monomer units greater than or equal to 20.

7. A method for obtaining an ultrasound contrast image of body tissue comprising:  
administering into a body a composition useful as an ultrasound contrast agent  
comprising microbubbles encapsulating a gas within a shell made from intermolecular regions of  
blended compounds, said compounds comprised of polar head groups linked to straight-chained  
hydrophobic groups of differing chain lengths said hydrophobic chains oriented toward the gas  
phase, whereby the longer chain lengths assemble beneath the shorter chains thereby stabilizing  
the shell and taking an ultrasound image of the desired tissue.

8. The method of Claim 7 wherein the bipolar compounds have the structure:



where  $R_1$ ,  $R_2$  and  $R_3$  are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyldisulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where  $R_1$  is greater than  $R_2$  and  $R_1$  is greater than or equal to  $R_3$ ;  $R_3$  has one or more such hydrophobic groups having the same or different lengths;  $X$  is a linker connecting the hydrophobic group to the polar head group;  $Z$  is a polar head group selected from the group consisting of  $\text{CO}_2\text{-M}^+$ ,  $\text{SO}_3\text{-M}^+$ ,  $\text{SO}_4\text{-M}^+$ ,  $\text{PO}_3\text{-M}^+$ ,  $\text{PO}_4\text{-M}^{+2}$ ,  $\text{N(R)}_4^+$ , a pyridinium or substituted pyridinium group, and a zwitterionic group;  $R$  is selected from the group consisting of  $\text{-H}$ ,  $\text{-CH}_3$ , alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and  $Z'$  is a nonionic group.

9. The method of Claim 8 wherein  $R_1$ ,  $R_2$  and  $R_3$  are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

10. The method of Claim 8 wherein  $X$  is selected from the group consisting of  $\text{-(CH}_2\text{)}_m^-$ ,  $\text{-(CH}_2\text{)}_m\text{CO}_2\text{(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{CONH(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{NHCONH(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{OCONH(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{O(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{NH(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{N[(CH}_2\text{)}_m]_2^-$ ,  $\text{-(CH}_2\text{)}_m\text{S(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m^-$ ,  $\text{-(CH}_2\text{)}_m\text{SO(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{SO}_2\text{(CH}_2\text{)}_n^-$ ,  $\text{-(CH}_2\text{)}_m\text{NH(CH}_2\text{)}_n\text{CO}_2\text{(CH}_2\text{)}_o^-$ ,  $\text{-[(CH}_2\text{)}_m]_2\text{N(CH}_2\text{)}_n\text{CONH(CH}_2\text{)}_o^-$ , where  $m$ ,  $n$ , and  $o$  are the same or different and are less than 5, DL-lysine, aspartic acid, glutamic acid, serine, cysteine,

homocysteine, cystine, serinol, itaconic acid, tigilic acid, maleic acid, DL-malic acid, succinic acid, tartaric acid, malonic acid, citric acid, phthalic acid, terephthalic acid, N,N-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-hydroxyethyl)glycine, 3-[N,N-bis(2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-tris[hydroxymethyl]methyl-3-aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine.

11. The method of Claim 8 wherein Z' is selected from the group consisting of polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides, polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and composites thereof.

12. The method of Claim 8 wherein Z' is poly(ethyleneglycol) with the number of ethyleneglycol monomer units greater than or equal to 20.

13. The method of Claim 7 wherein the tissue is the heart and the image is a myocardial perfusion image.

14. A method for measuring pressure or fluid flow rates in a closed system comprising:

administering a composition useful for measuring pressure or fluid flow rates comprising microbubbles encapsulating a gas within a shell made from intermolecular regions of blended compounds, said compounds comprised of polar head groups linked to straight-chained hydrophobic groups of differing chain lengths said hydrophobic chains oriented toward the gas phase, whereby the longer chain lengths assemble beneath the shorter chains thereby stabilizing the shell into a closed system, measuring the acoustic changes with frequency for the system; and calculating the change in pressure or change in fluid flow rate.

15. The method of Claim 14 wherein the bipolar compounds have the structure:

$R_1-X-Z$ ;

$R_2-X-Z$ ;

and  $R_3-X-Z'$

where  $R_1$ ,  $R_2$  and  $R_3$  are hydrophobic groups selected from the group consisting of straight-chained alkyls, alkylethers, alkylthioethers, alkyldisulfides, polyfluoroalkyls, and polyfluoroalkylethers having a carbon chain length greater than or equal to 16 and less than or equal to 32 and where  $R_1$  is greater than  $R_2$  and  $R_1$  is greater than or equal to  $R_3$ ;  $R_3$  has one or more such hydrophobic groups having the same or different lengths; X is a linker connecting the hydrophobic group to the polar head group; Z is a polar head group selected from the group consisting of  $CO_2-M^+$ ,  $SO_3^-M^+$ ,  $SO_4^-M^+$ ,  $PO_3^-M^+$ ,  $PO_4^-M^+$ ,  $N(R)_4^+$ , a pyridinium or substituted pyridinium group, and a zwitterionic group; R is selected from the group consisting of -H, -CH<sub>3</sub>, alkyl, cycloalkyl, substituted cycloalkyls containing one or more heteroatoms, and benzyl and can be the same or different; and Z' is a nonionic group.

16. The method of Claim 15 wherein  $R_1$ ,  $R_2$  and  $R_3$  are straight-chained alkyl groups having from about 20 to 30 carbon atoms.

17. The method of Claim 15 wherein X is selected from the group consisting of -  
(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>CONH(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>NHCONH(CH<sub>2</sub>)<sub>n</sub>-,  
-(CH<sub>2</sub>)<sub>m</sub>OCONH(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>O(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>NH(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>N[(CH<sub>2</sub>)<sub>m</sub>]<sub>2</sub>-,  
-(CH<sub>2</sub>)<sub>m</sub>S(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>-, -(CH<sub>2</sub>)<sub>m</sub>SO(CH<sub>2</sub>)<sub>n</sub>-, -(CH<sub>2</sub>)<sub>m</sub>SO<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>-,  
-(CH<sub>2</sub>)<sub>m</sub>NH(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>(CH<sub>2</sub>)<sub>o</sub>-, -[(CH<sub>2</sub>)<sub>m</sub>]<sub>2</sub>N(CH<sub>2</sub>)<sub>n</sub>CONH(CH<sub>2</sub>)<sub>o</sub>-, where m, n, and o are the same or different and are less than 5; DL-lysine, aspartic acid, glutamic acid, serine, cysteine, homocysteine, cystine, serinol, itaconic acid, tigilic acid, maleic acid, DL-malic acid, succinic

acid, tartaric acid, malonic acid, citric acid, phthalic acid, terephthalic acid, N,N-bis[2-hydroxyethyl]-2-aminoethanesulfonic acid, N,N-bis(2-hydroxyethyl)glycine, 3-[N,N-bis(2-hydroxyethyl)amino]-2-hydroxypropanesulfonic acid, N-tris[hydroxymethyl]methyl-3-aminopropanesulfonic acid, and N-tris[hydroxymethyl]glycine.

18. The method of Claim 15 wherein Z' is selected from the group consisting of polysorbates, polyglycerols, polypeptides, polynucleotides, polysaccharides, polyvinylpyrrolidones, polyvinylalcohols, polyethyleneglycols, and composites thereof.

19. The method of Claim 15 wherein Z' is poly(ethyleneglycol) with the number of ethyleneglycol monomer units greater than or equal to 20.

20. The method of Claim 14 wherein the closed system is the body circulatory system.